DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

DISTRICT ADDRESS AND PHONE NUMBER	DATE(S) OF INSPECTION
19701 Fairchild Irvine, CA 92612-2445 (949)608-2900 Fax:(949)608-4417	7/14/2016-8/1/2016* FEI NUMBER 3012242764

NAME AND TITLE OF INDIVIDUAL TO WHOM REPORT ISSUED
Kang (NMI) Zhang, M.D., Ph.D. , Sponsor-Clinical Investigator

FIRM NAME	STREET ADDRESS
Kang Zhang, M.D., Ph.D.	9415 Campus Point Dr., Room E214
CITY, STATE, ZIP CODE, COUNTRY La Jolla, CA 92093-0946	TYPE ESTABLISHMENT INSPECTED Sponsor-Investigator

This document lists observations made by the FDA representative(s) during the inspection of your facility. They are inspectional observations, and do not represent a final Agency determination regarding your compliance. If you have an objection regarding an observation, or have implemented, or plan to implement, corrective action in response to an observation, you may discuss the objection or action with the FDA representative(s) during the inspection or submit this information to FDA at the address above. If you have any questions, please contact FDA at the phone number and address above.

DURING AN INSPECTION OF YOUR FIRM I OBSERVED:

In relation to a clinical trial conducted under a protocol titled, Protocol # (b) (4) **,** "(b) (4) "

Protocol Version 1, dated 01/24/09

Protocol Version 2, dated 04/05/12

Protocol Version 3.5, dated 01/28/13

SPONSOR

OBSERVATION 1

Failure to monitor the progress of an investigation conducted under your IND.

Specifically, there was no Monitoring Procedures/Plan or any documentation, such as monitoring reports or logs to show that the investigational sites were monitored. There was no documentation to verify that the investigational sites have conducted the clinical trials according to the protocol requirements.

OBSERVATION 2

Failure to submit to FDA an annual report of the investigation.

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	Natalie J Ayoub, Investigator - Dedicated Food Cadre X Natalie J Ayoub Natalie J Ayoub Investigator - Dedicated Food Cadre Signed by Natalie J Ayoub -5	8/1/2016

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Specifically, you did not submit to FDA an annual report for IND (b) (4) associated with Protocol # (b) (4) within 60 days of the anniversary date 02/05/11 that the IND went in effect. FDA received Protocol #(b) (4) under IND (b) (4) on 04/25/11. You did not submit an annual report in 2012, 2014, 2015, and 2016. The IND is still active and has not been closed.

CLINICAL INVESTIGATOR

OBSERVATION 3

Failure to assure that an IRB was responsible for the initial and continuing review and approval of a clinical study.

Specifically, on December 7, 2012, the Investigational Review Board (IRB) for Protocol # (b) (4) notified the Principal Investigator "Effective immediately, suspension of new enrollment for ALL of the PI's active research trials at UCSD". On 08/26/13, the IRB lifted the enrollment suspension on the Principal Investigator. During the enrollment suspension period, the following subjects were enrolled in Protocol # (b) (4):

1) Subject (b) (6) was enrolled and received the study drug on 06/17/13. The subject conducted their Month 1 visit on 07/22/13 and Month 2 visit on 08/19/13. The study drug was not administered during the Month 1 and Month 2 visits.
2) Subject (b) (6) was enrolled and received the study drug on 08/12/13.
3) Subject (b) (6) was enrolled and received the study drug on 08/13/13.

OBSERVATION 4

An investigation was not conducted in accordance with the investigational plan.

Specifically, the following observations were deviations from the protocol:

A. All versions of the protocol had Section 4.1.2 Inclusion Criteria, Item 3, which required "(b) (4)

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(b) (4) " and, Item 4, which required "(b) (4) " to be included.

a) The following subjects lost (b) (4) letters or less from baseline best vision:
   1) Subject (b) (6)
   2) Subject
   3) Subject
   4) Subject
   5) Subject
   6) Subject
   7) Subject

b) The following subjects had records with the following readings:
   1) Subject (b) (6) was a non-(b) (4) patient whose Baseline visit, dated 08/12/11, documented visual acuity through pinhole of 20/60 in the right eye. The Day 0 visit, dated 11/28/11, documented visual acuity through pinhole of 20/50 in the right eye (study eye). The subject did not meet Inclusion Criteria Item 3 & 4.
   2) Subject (b) (6) was a (b) (4) patient whose Baseline visit, dated 09/20/11, documented visual acuity 20/25 -2 in the right eye. The Day 0 visit, dated 02/13/12, documented visual acuity 20/32 -2. The subject did not meet Inclusion Criteria Item 3 & 4.
   3) Subject (b) (6) was a (b) (4) patient whose Baseline visit is documented to occur on 03/25/13. The Day 0 visit occurred on 08/12/13. The subject did not meet Inclusion Criteria Item 3.

B. Amendment 2 and 3 of the protocol had section 4.1.2 Inclusion Criteria, Item 5, which required "(b) (4) . Subject (b) (6) had a baseline Snellen VA of 20/25 for the study eye OD on 05/30/13; therefore, the subject did not meet inclusion criteria Item 5.

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C. All versions of the protocol had section 4.1.1 Subject Selection referencing Appendix A documenting the study flow chart which required EDTRS BCVA, SD-OCT, and FA to be obtained at the Baseline period and Day 0/Screening visit. All (b)(4) subject records were reviewed. The following subjects were missing protocol required examinations needed to determine inclusion/exclusion criteria for the study:

1) Subject (b)(6) did not have EDTRS BCVA, SD-OCT, and FA conducted on the study eye for the Day 0/Screening visit.
2) Subject (b)(6) did not have SD-OCT and FA for the Baseline visit.
3) Subject did not have SD-OCT and FA for the Baseline visit.
4) Subject did not have EDTRS BCVA, SD-OCT, and FA for the Baseline visit.
5) Subject did not have SD-OCT and FA for the Baseline visit.
6) Subject did not have SD-OCT and FA for the Baseline visit.

D. All versions of the protocol section 4.5.2 Early Termination Assessments require (b)(4) [redacted]." An early termination visit was not conducted for Subjects (b)(6) [redacted].

OBSERVATION 5

The informed consent document does not include the required statement: "A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Specifically, all versions of your informed consent form does not contain the required clinical trial statement.

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OBSERVATION 6

Investigational records were not retained for a period of two years following discontinuance of the investigation and notification of FDA.

Specifically, the following records were not retained:

E. Refrigerated study drug temperature log from 07/19/13 to the end of the study.

F. Informed Consent Form (ICF) signed by Subject (b) (6) on 07/16/13. The source document contains a Note to File stating the subject signed the incorrect version of the ICF; however, the ICF form cannot be located.

G. Subject (b) (6) 's source documents did not contain SD-OCT and FA records for the Month 12 visit, despite documentation of it being conducted.

H. Subject (b) (6) 's source documents did not contain SD-OCT and FA records for the Baseline visit, despite documentation of it being conducted during the previous (b) (4) study visit.

OBSERVATION 7

Investigational drug disposition records are not adequate with respect to quantity.

Specifically, the disposition of the expired study drug is not adequately documented for the following:

I. A destruction record, dated 05/09/12, documenting destruction via chemical waste of (b) (4) of the expired study drug does not document the lots of the expired investigational drugs destroyed. Additionally, the study drug accountability log documents (b) (4) units of Lot # (b) (4) expiring on (b) (4) (b) (4) units of Lot # (b) (4) expiring on (b) (4), and (b) (4) units of Lot # (b) (4) expired on (b) (4), totaling (b) (4) units of the investigational drug with an expiration date prior to 05/09/12. (b) (4) units are unaccounted for.

J. You do not have documentation of the accountability of the received (b) (4) unit of unused, expired investigational drugs, Lot (b) (4), expiration date (b) (4).

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*DATES OF INSPECTION

7/14/2016(Thu),7/15/2016(Fri),7/18/2016(Mon),7/19/2016(Tue),7/20/2016(Wed),7/21/2016(Thu),7/22/2016(Fri),7/25/2016(Mon),7/28/2016(Thu),8/01/2016(Mon)

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